



UNIVERSITY of MARYLAND
CENTER FOR DIABETES AND
ENDOCRINOLOGY

Obesity and Its Impact on Diabetes

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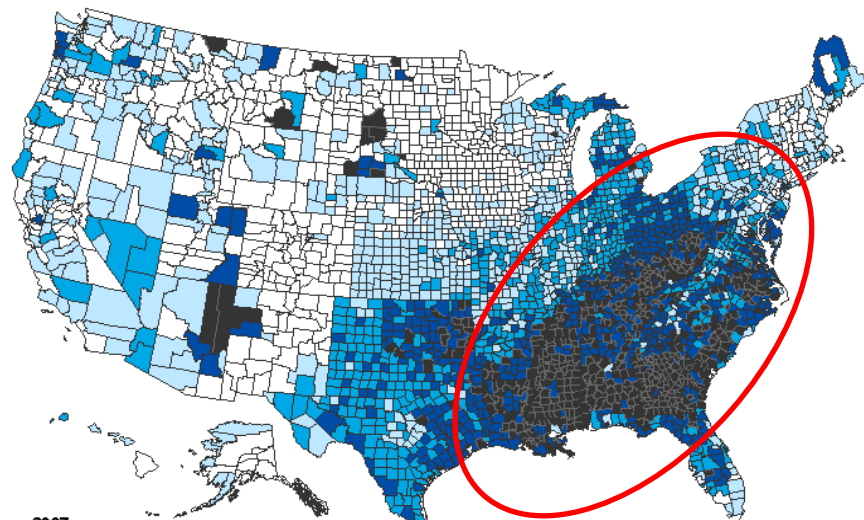


June 26, 2014

Objectives

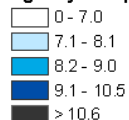
- **Discuss the impact of obesity on diabetes morbidity and mortality**
- **Describe how obesity and diabetes are interrelated**
- **Discuss current and effective strategies for addressing comorbid diabetes and obesity**



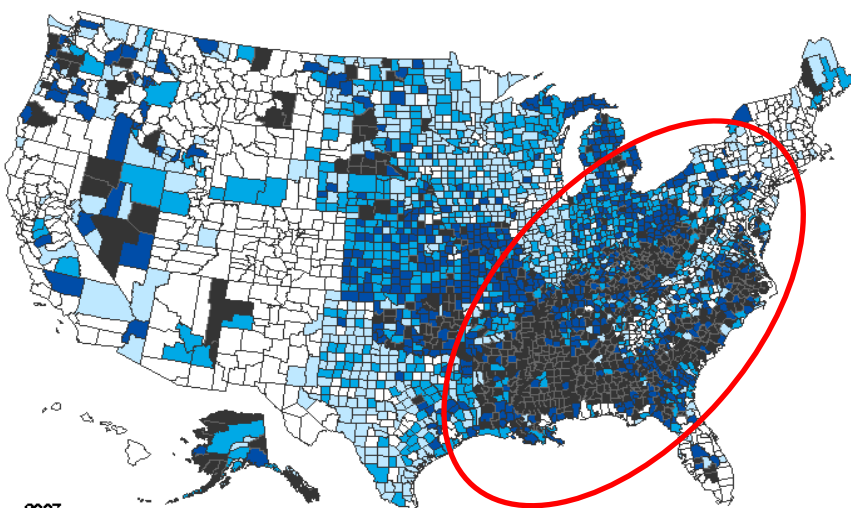


2007

Age-adjusted percent of adults ≥ 20 years old with diabetes

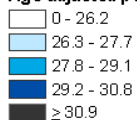


Age-adjusted percentage of adults aged ≥ 20 years who are obese, 2007
Source: MMWR 58:1259-1263, 2009



2007

Age-adjusted percent of adults ≥ 20 years old who are obese



Age-adjusted percentage of adults aged ≥ 20 years with diagnosed diabetes, 2007
Source: MMWR 58:1259-1263, 2009c

OBESITY

85 million adults, 2011-2012

34.4 % Overweight

BMI 25-29.9

33.9 % Obese

BMI >30

5.7% Extremely obese

BMI >40

1.68 million Maryland residents (28.8%)

DIABETES

86 million adults with pre-diabetes (37%)

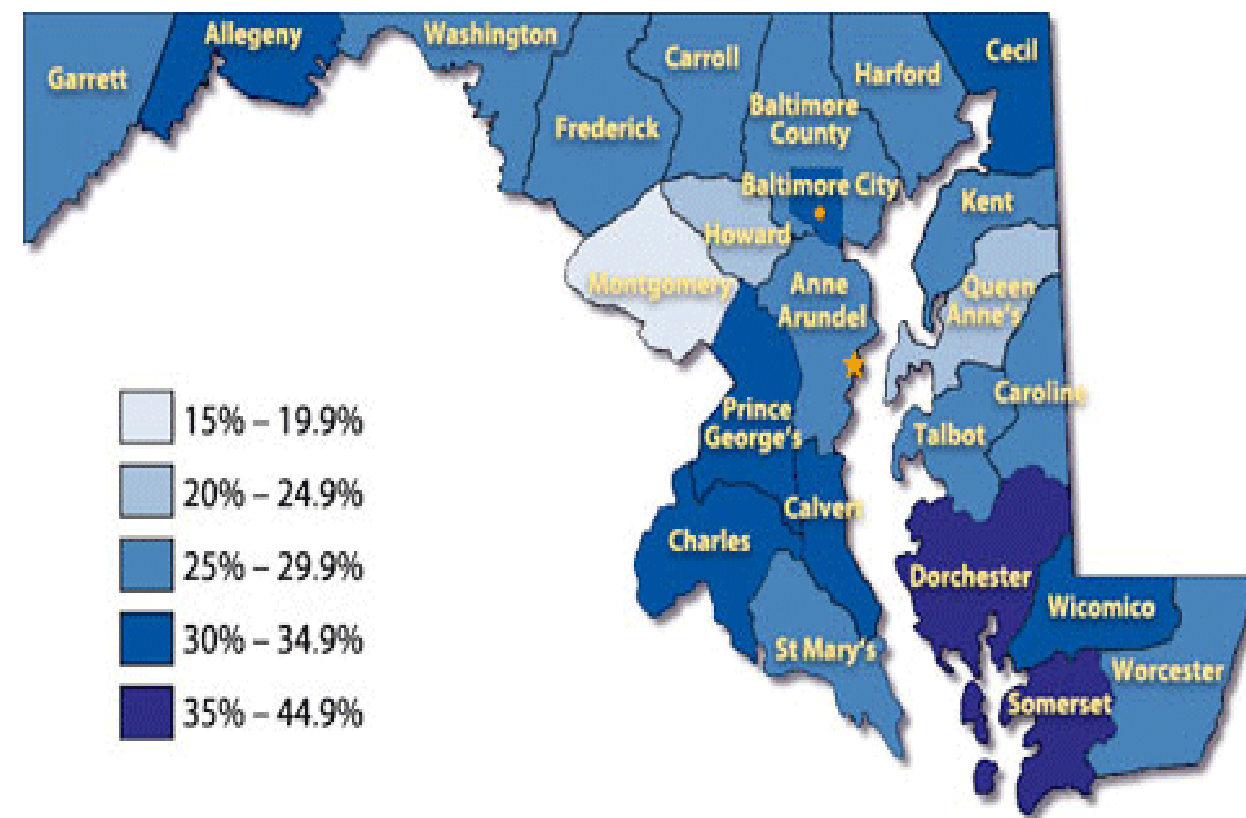
29.1 million adults and children with diabetes (9.3%)

Over 85% of diabetes patients are overweight, over 50% are obese

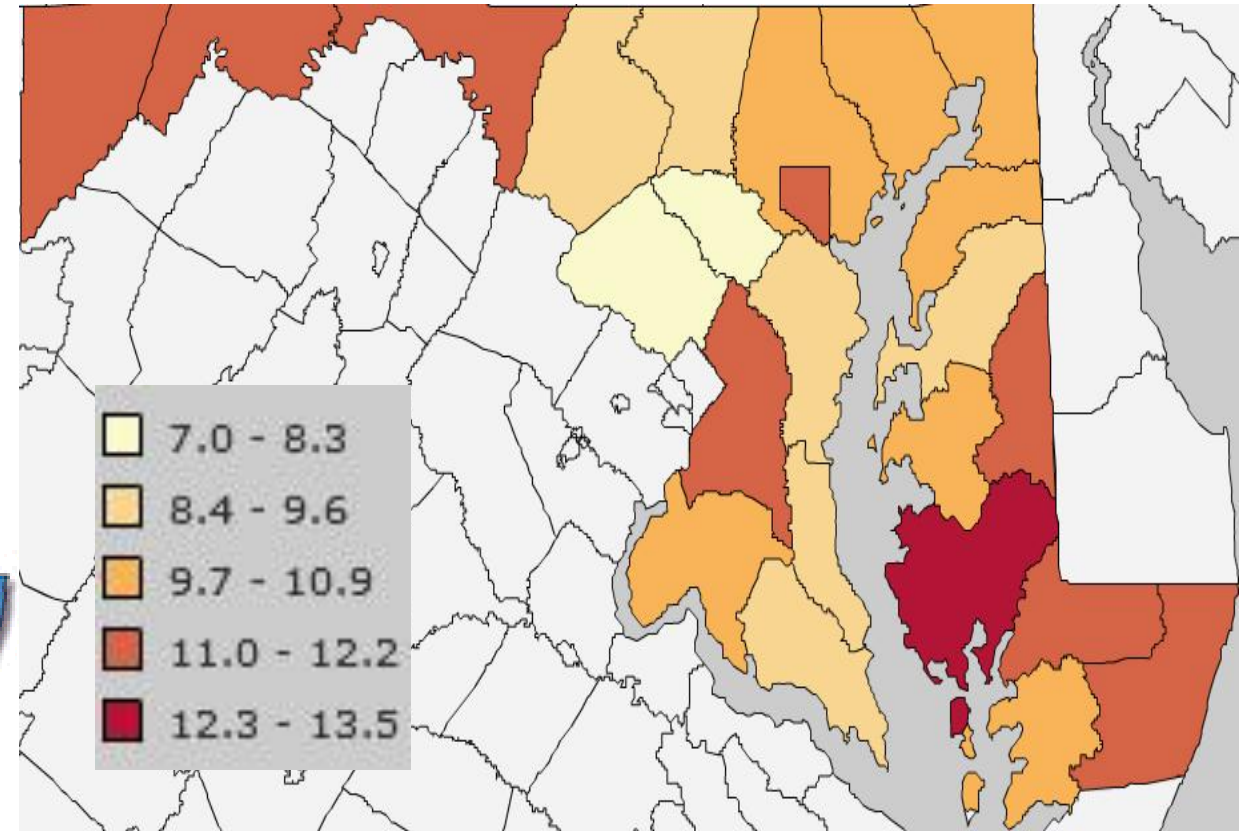
~400,000 Maryland residents

JAMA. 2014;311(8):806-814; Healthyamericans.org; <http://www.diabetes.org/diabetes-basics/diabetes-statistics/>; CDC- MMWR Report. 11/2004; 53: 1066-1064

Obesity and Diabetes in Maryland

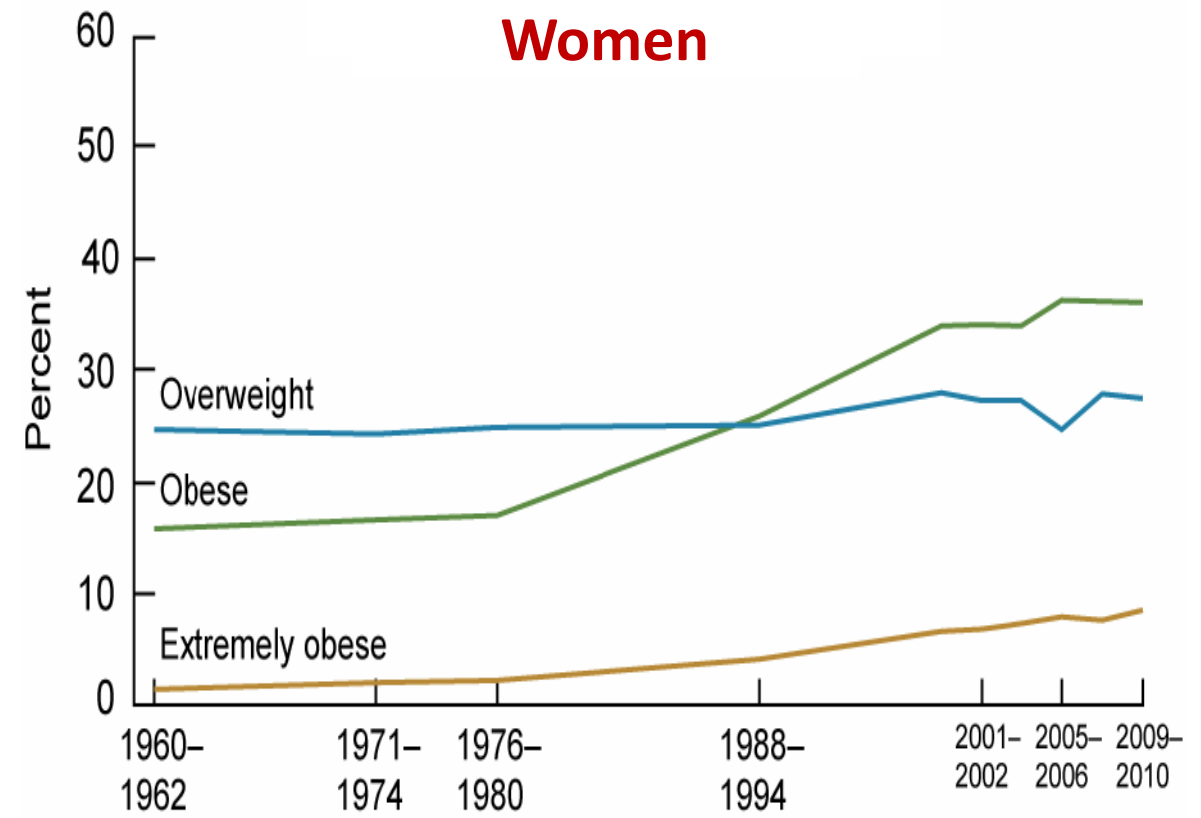
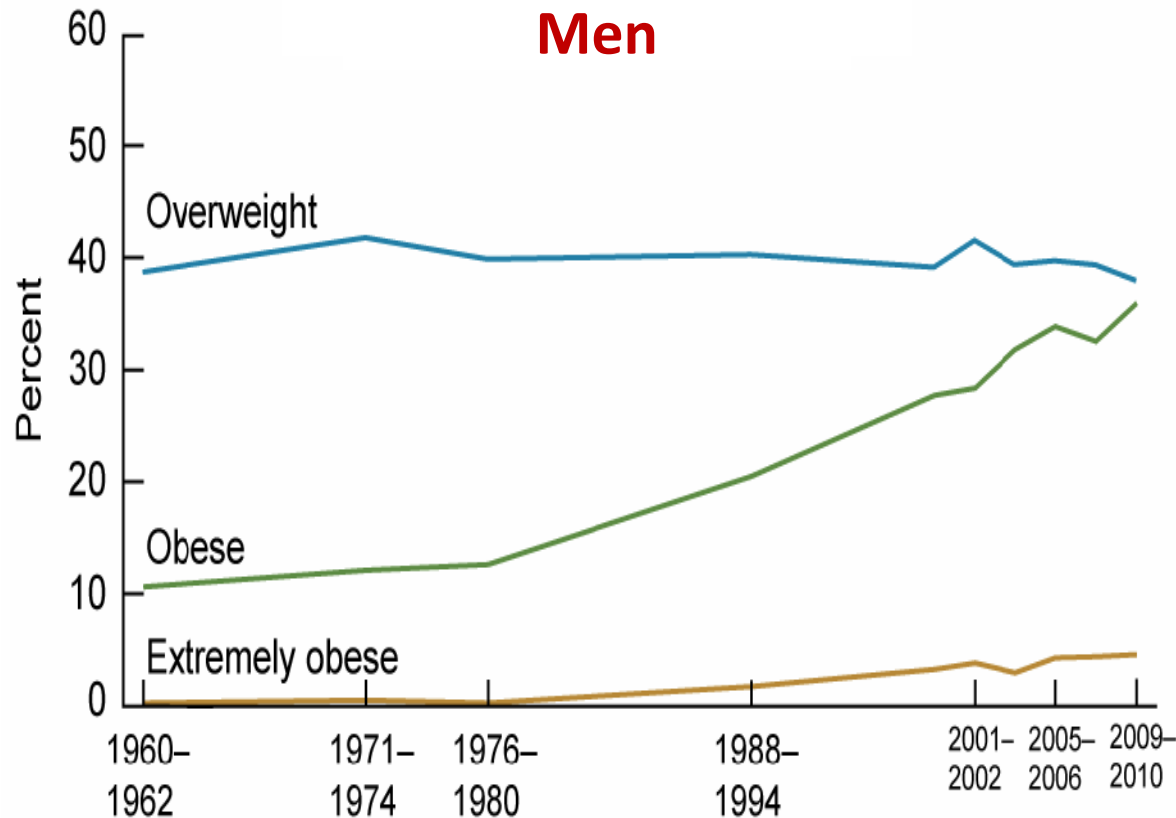


OBESITY

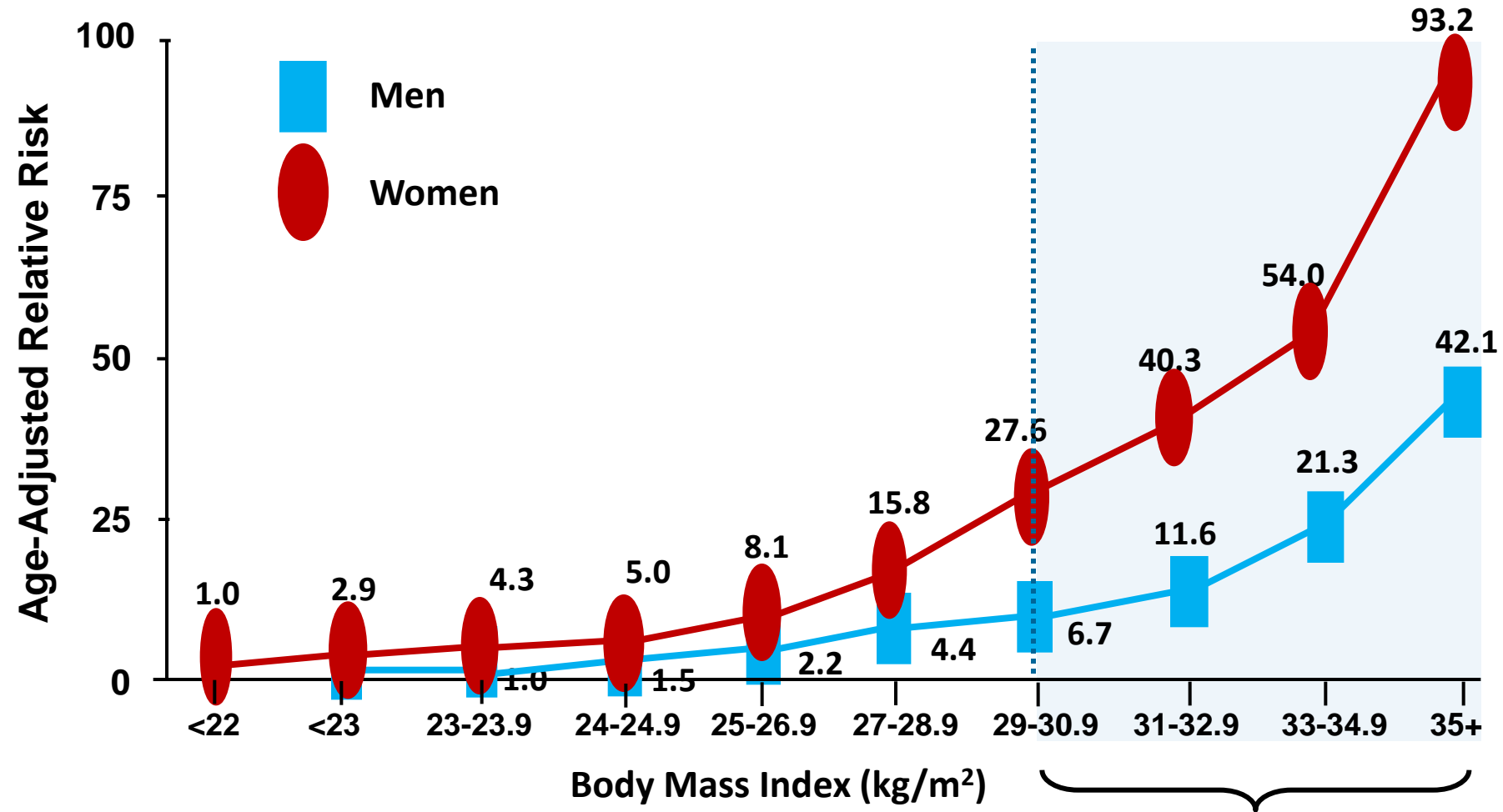


DIABETES

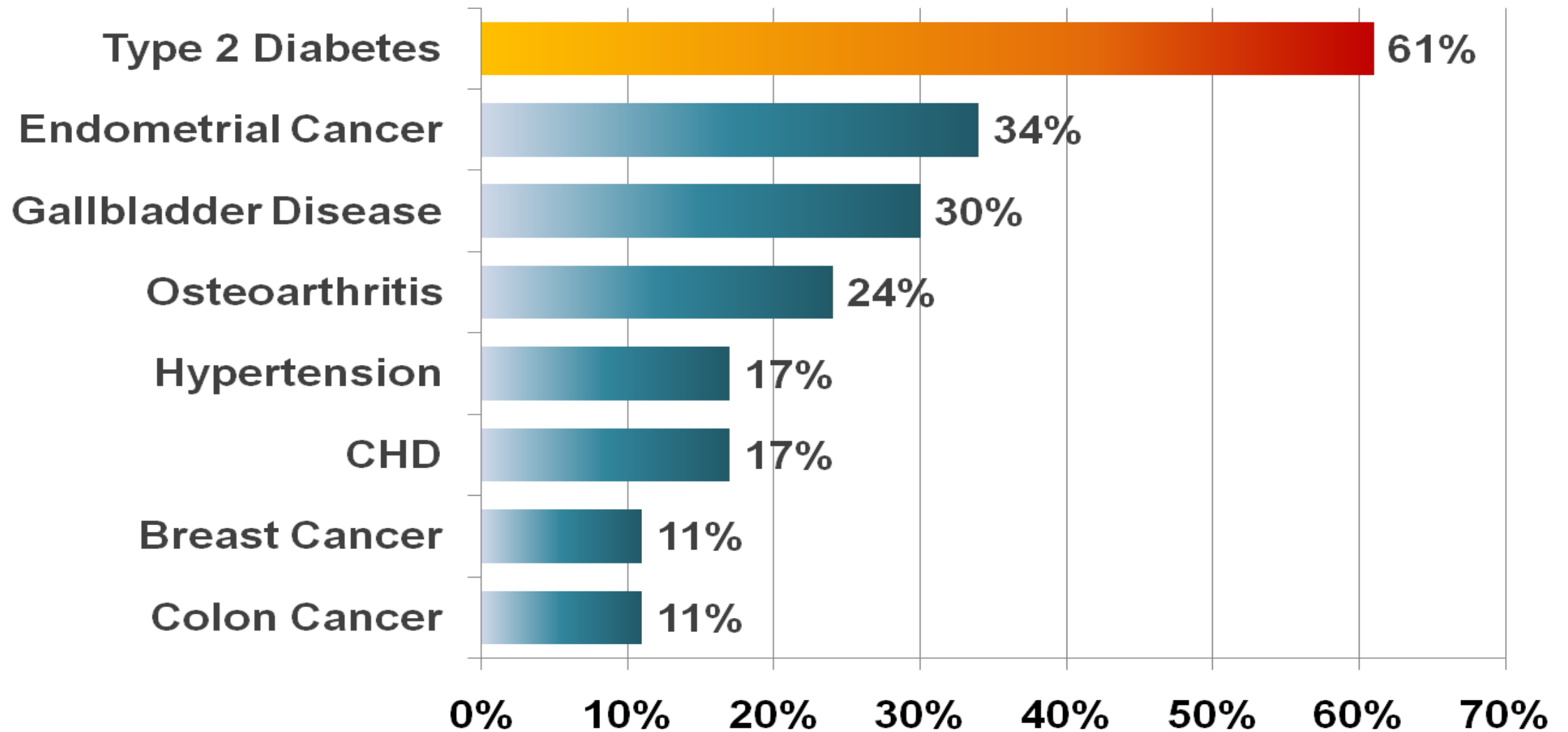
Overweight and Obesity Trends Among U.S. Adults aged 20-74 years (1960-2010)



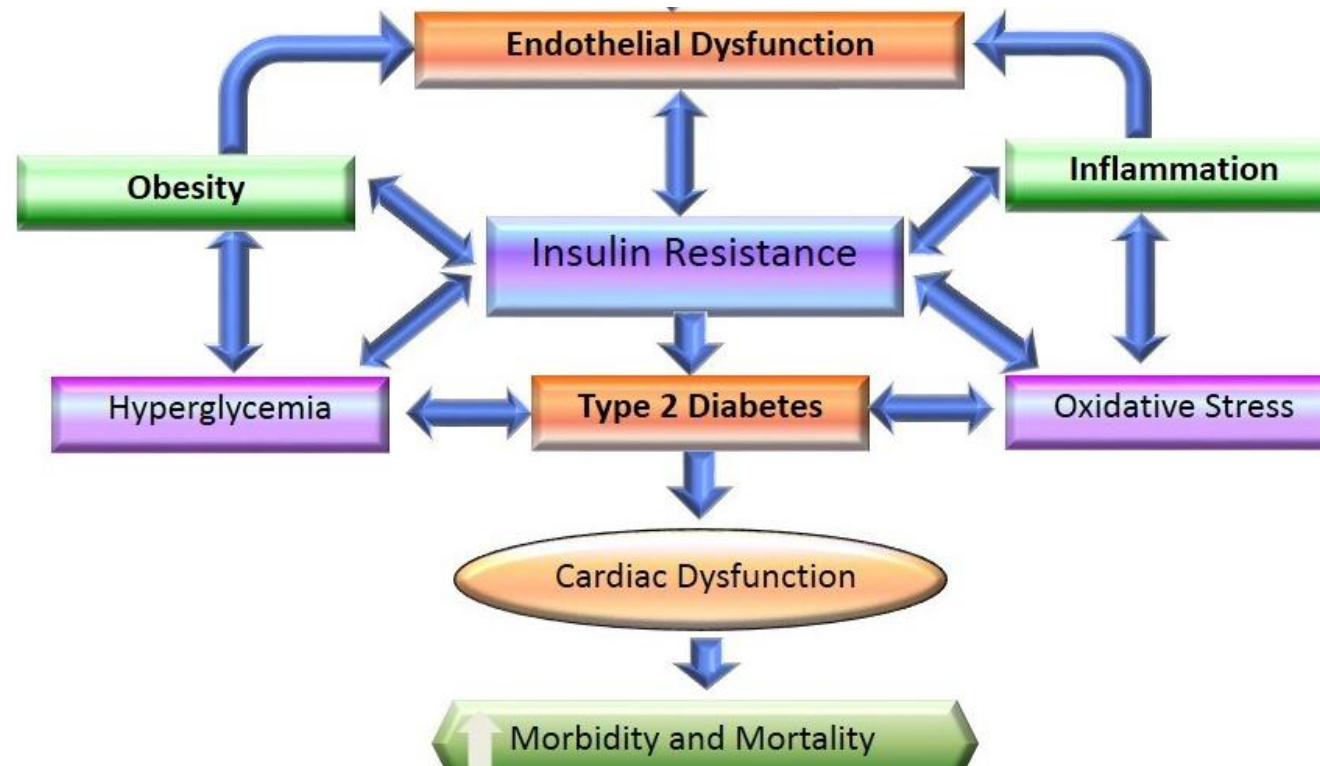
Relationship Between BMI and Risk of Type 2 Diabetes Mellitus



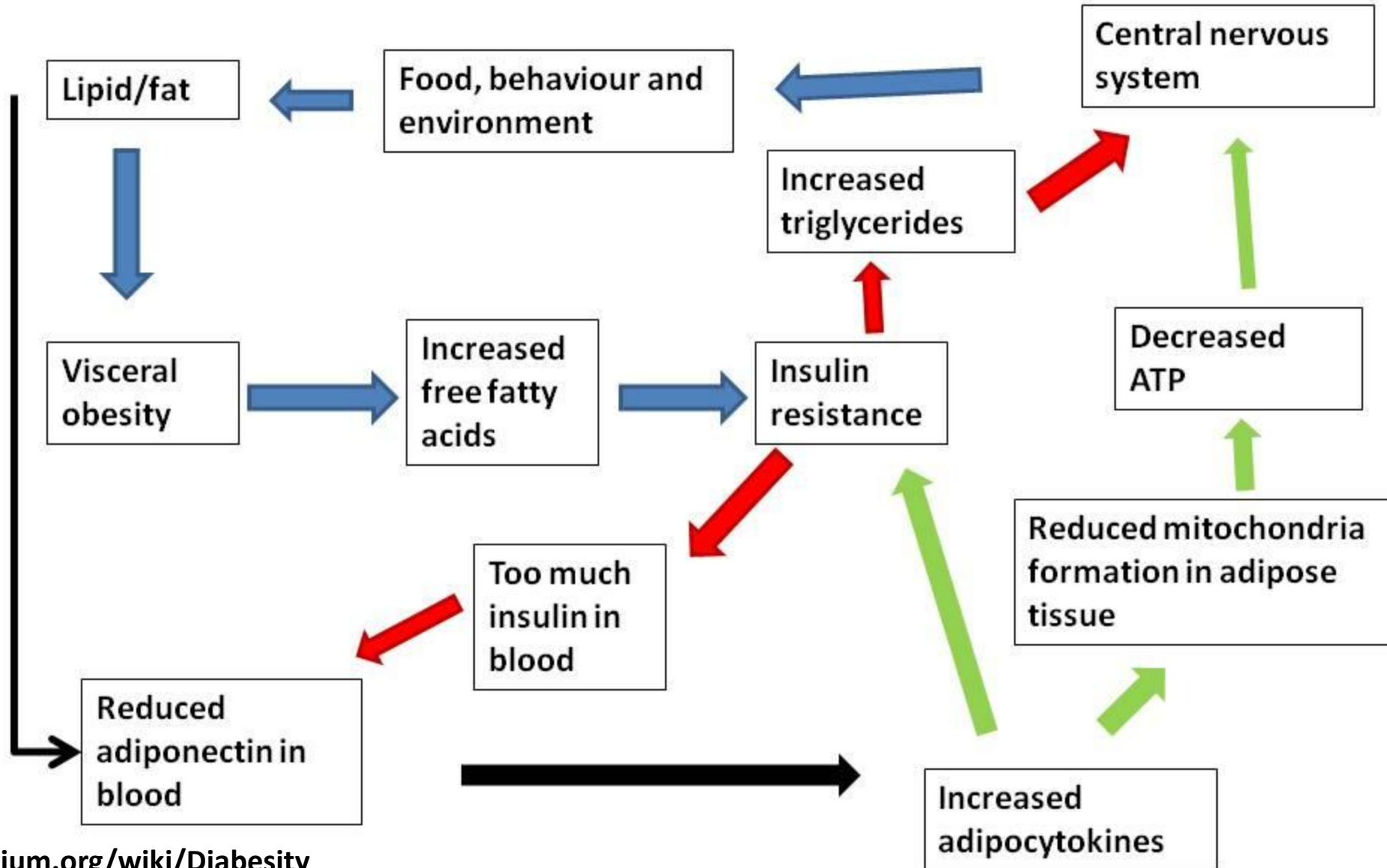
Disease Prevalence Attributable to Obesity



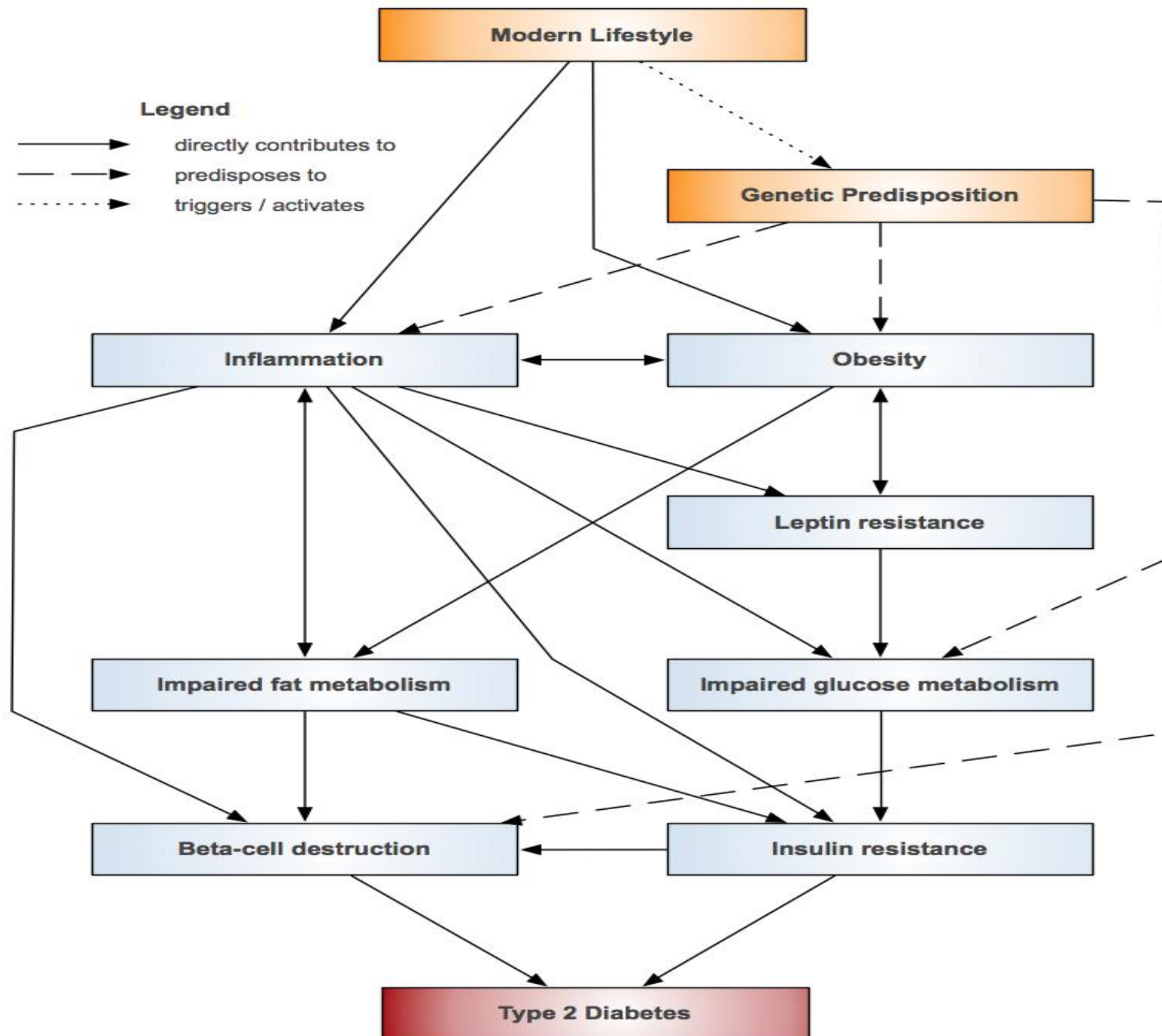
Factors linking Type 2 Diabetes and Obesity



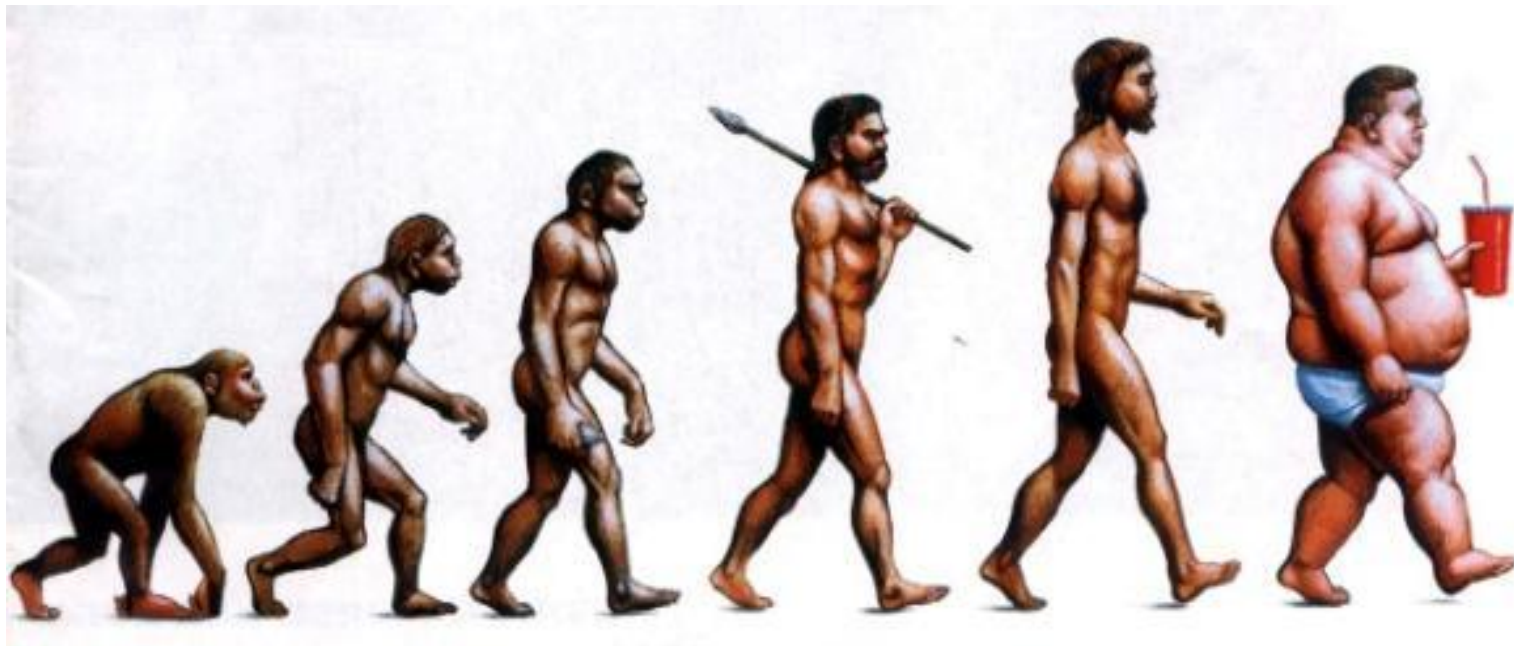
Factors linking Type 2 Diabetes and Obesity



Factors linking Type 2 Diabetes and Obesity



Rationale for Treating Obesity

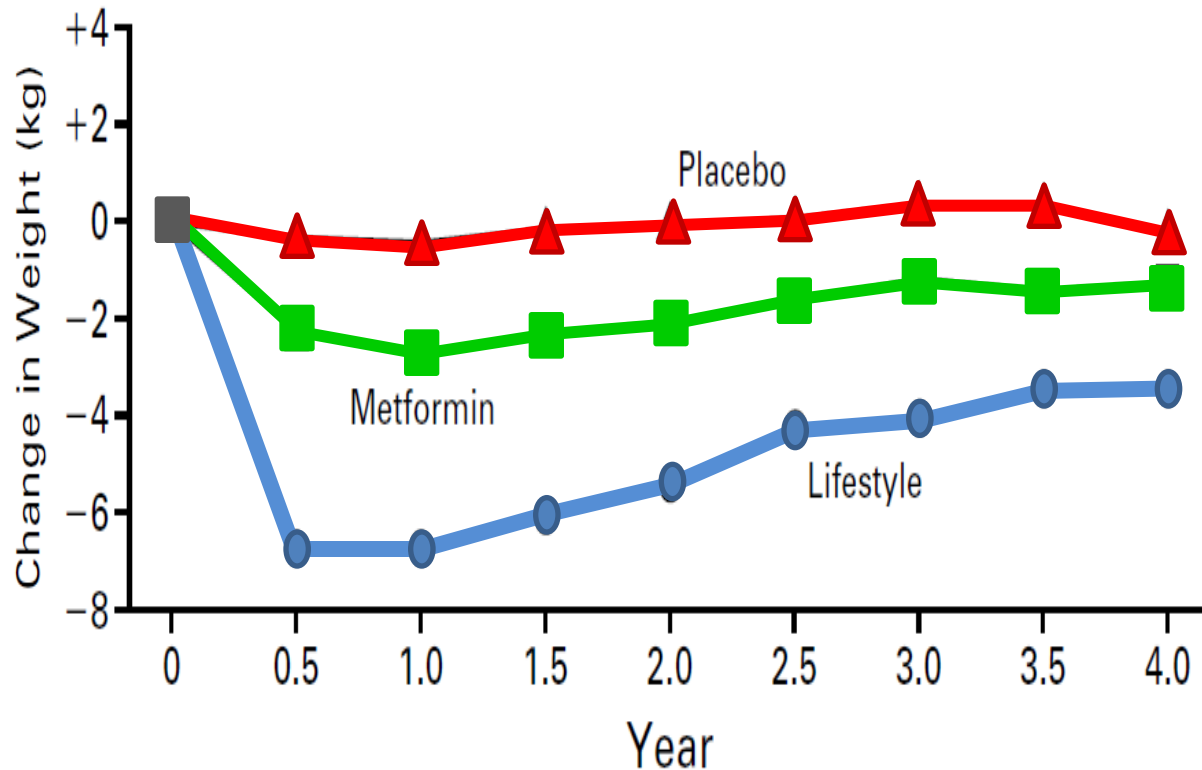


Weight Loss Reduces Risk of Type 2 DM in Subjects with IGT

Study	Type 2 DM Risk Reduction
Da Qing IGT and Diabetes Study ¹ (Diet and exercise)	42%
Finnish Diabetes Prevention Study ² (Diet and exercise)	58%
US Diabetes Prevention Program ³ (Diet and exercise)	58%
XENical in the Prevention of Diabetes in Obese Subjects (XENDOS) study ⁴ (orlistat)	37%

¹ Diabetes Care. 1997;20:537-44. ² N Engl J Med. 2001;344:1343-50. ³ N Eng J Med. 2002;346:393-403. ⁴ Diabetes Care. 2004 27:155-61

DPP: Intensive Lifestyle Intervention (ILI) and Weight Loss



3234 subjects in total; N = 1079 overweight/obese subjects with IGT (95-125 mg/dl), ages 25 - 84 yr

Diabetes Care. 2006;29:2102-2107; N Engl J Med 2002;346:393-403

ILI PROGRAM

GOAL: 7% loss initial weight

DIET

- Low fat (< 30% energy)
- Reduce energy (1200-1800 kcal)
- Conventional Foods, Ad libitum

ACTIVITY

- 150 min/week or more of moderate intensity exercise

COUNSELING

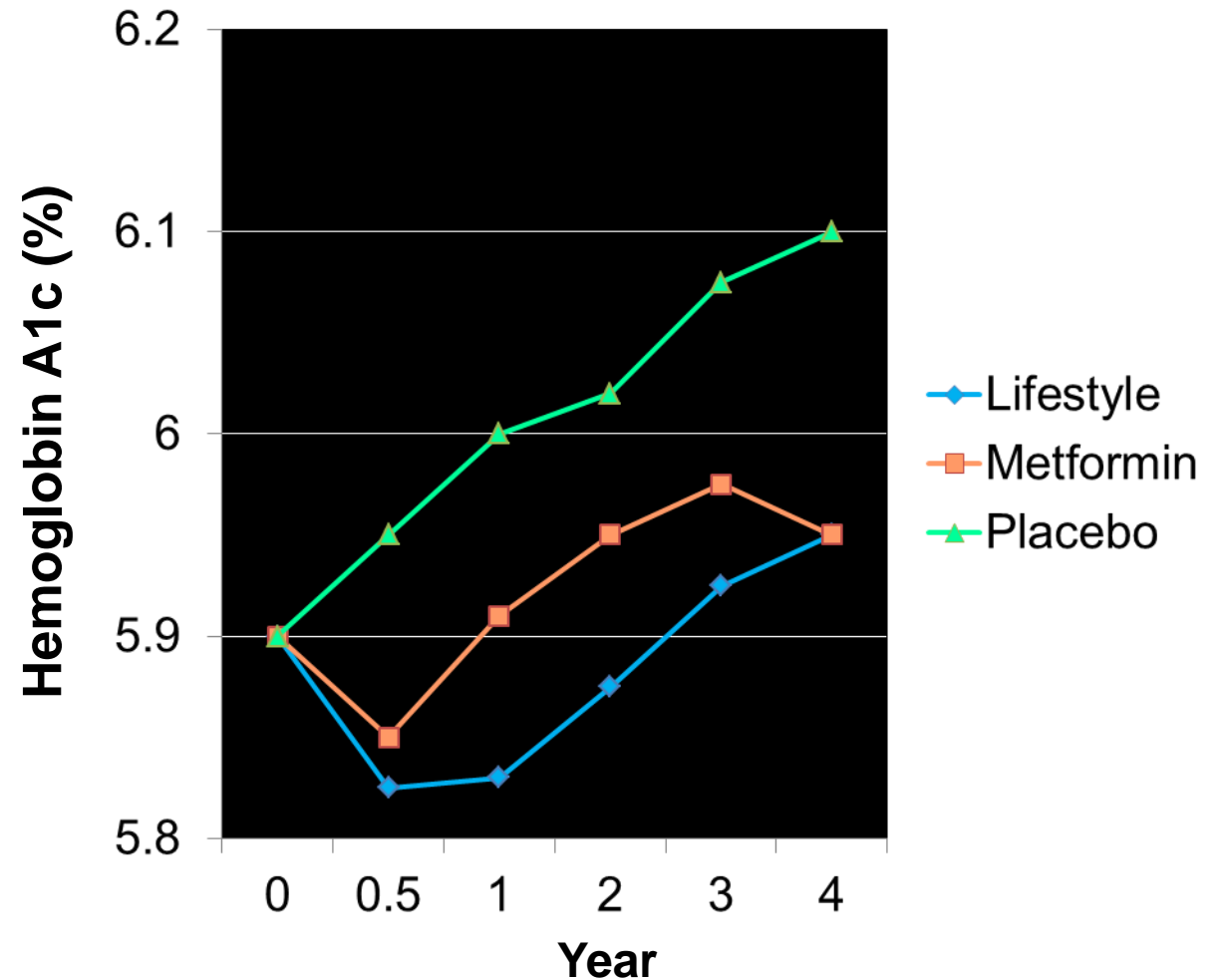
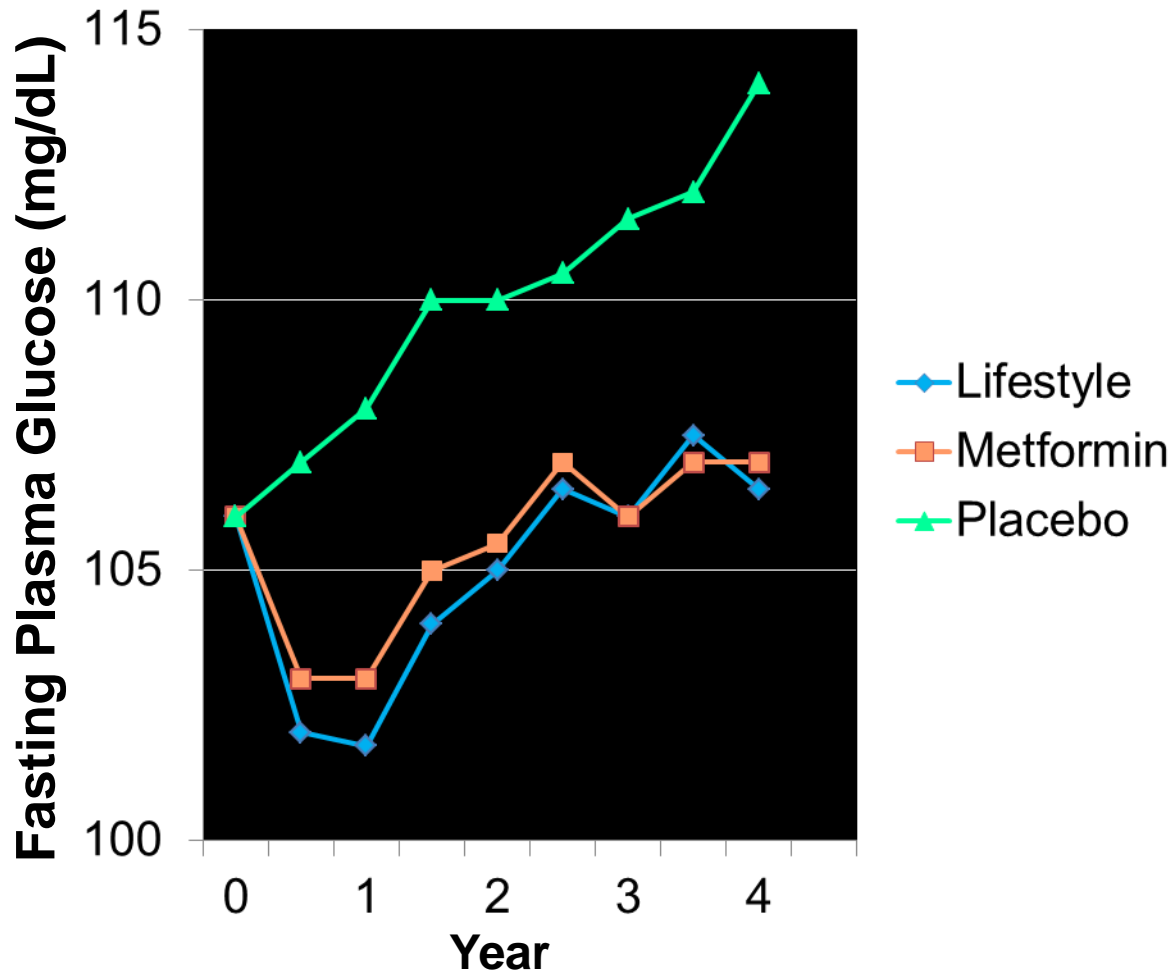
Weight Loss Phase (6 month):

- 16 individual visits every 1-2 wks

Maintenance Phase:

- Individual visits every 2 months
- Group classes (3 sessions/yr)
- Online resources

DPP: Intensive Lifestyle Intervention (ILI) and Glycemia

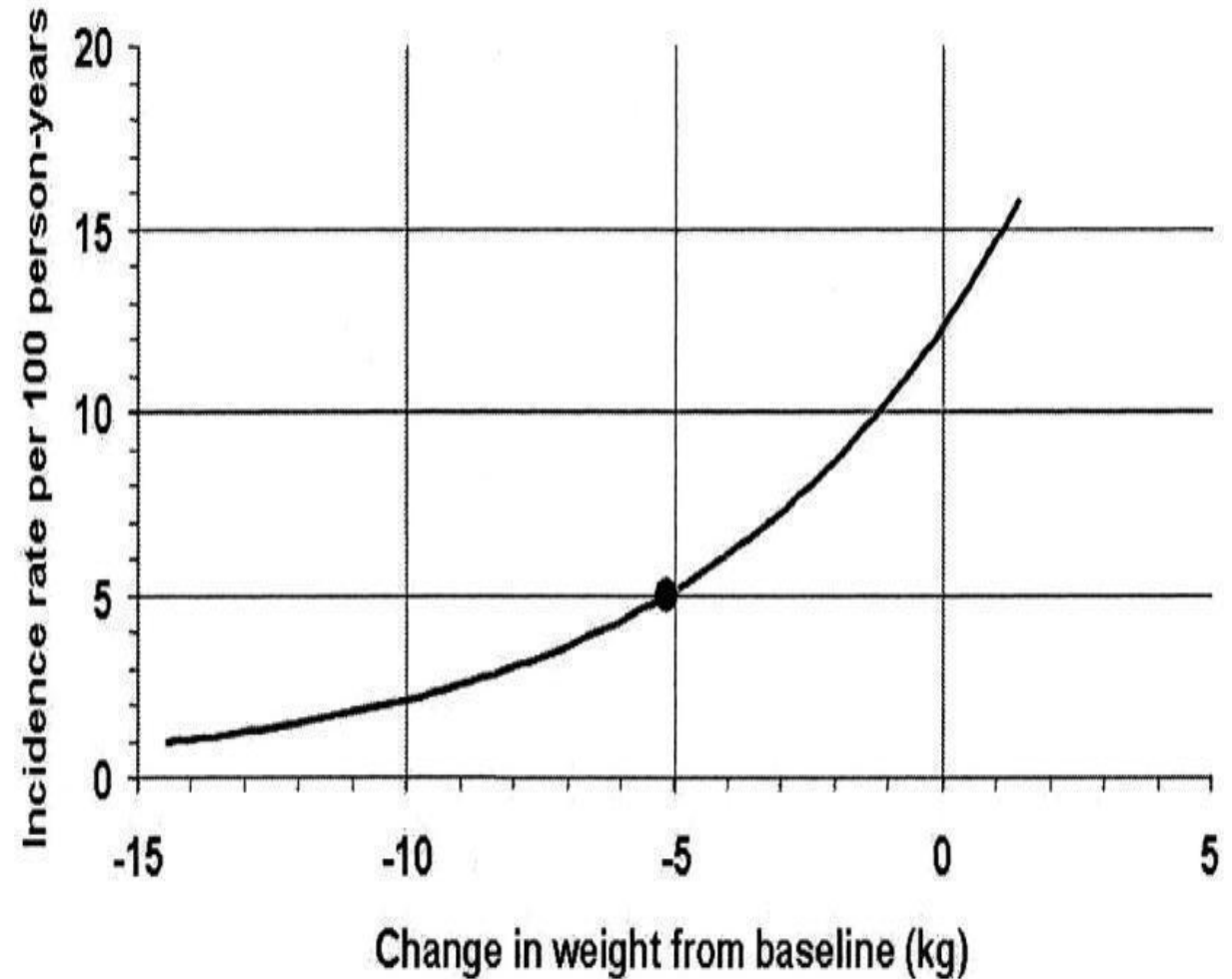


DPP: “Dose Response” of Diabetes Risk Reduction

N= 1079 overweight/obese subjects
(BMI > 24 kg/m²) with IGT (25 – 84
years of age)

**At 15 kg of weight loss, the risk
of diabetes is approximately 2%**

**For every 2.2 lbs (1 kg) of weight
loss, there is a 16% reduction in
the risk of developing diabetes**



Look AHEAD – Four Year Results



- Multicenter randomized clinical trial – **Can >7% weight loss with ↑ activity (170 min/wk) ↓ CVD events in overweight and obese subjects with type 2 diabetes?**
- Diet = 1200-1800 kcal/day, fat < 30% (10% saturated), used meal replacements

	Lifestyle Intervention Group (n=2,496)	Diabetes Support and Education Group (n=2,649)	P value
Weight Loss	-6.15%	-0.88%	<i>P</i> < 0.001
Treadmill Fitness	12.74%	1.96%	<i>P</i> < 0.001
Hemoglobin A1c	-0.36%	-0.09%	<i>P</i> < 0.001
Systolic BP	-5.33 mm Hg	-2.97 mm Hg	<i>P</i> < 0.001
Diastolic BP	-2.92 mm Hg	-2.48 mm Hg	<i>P</i> = 0.01
HDL	3.67	1.97 mg/dL	<i>P</i> < 0.001
Triglycerides	-25.56 mg/dL	-19.75 mg/dL	<i>P</i> < 0.001
LDL*	-11.27 mg/dL	-12.84 mg/dL	<i>P</i> = 0.009

Look AHEAD – Four Year Results



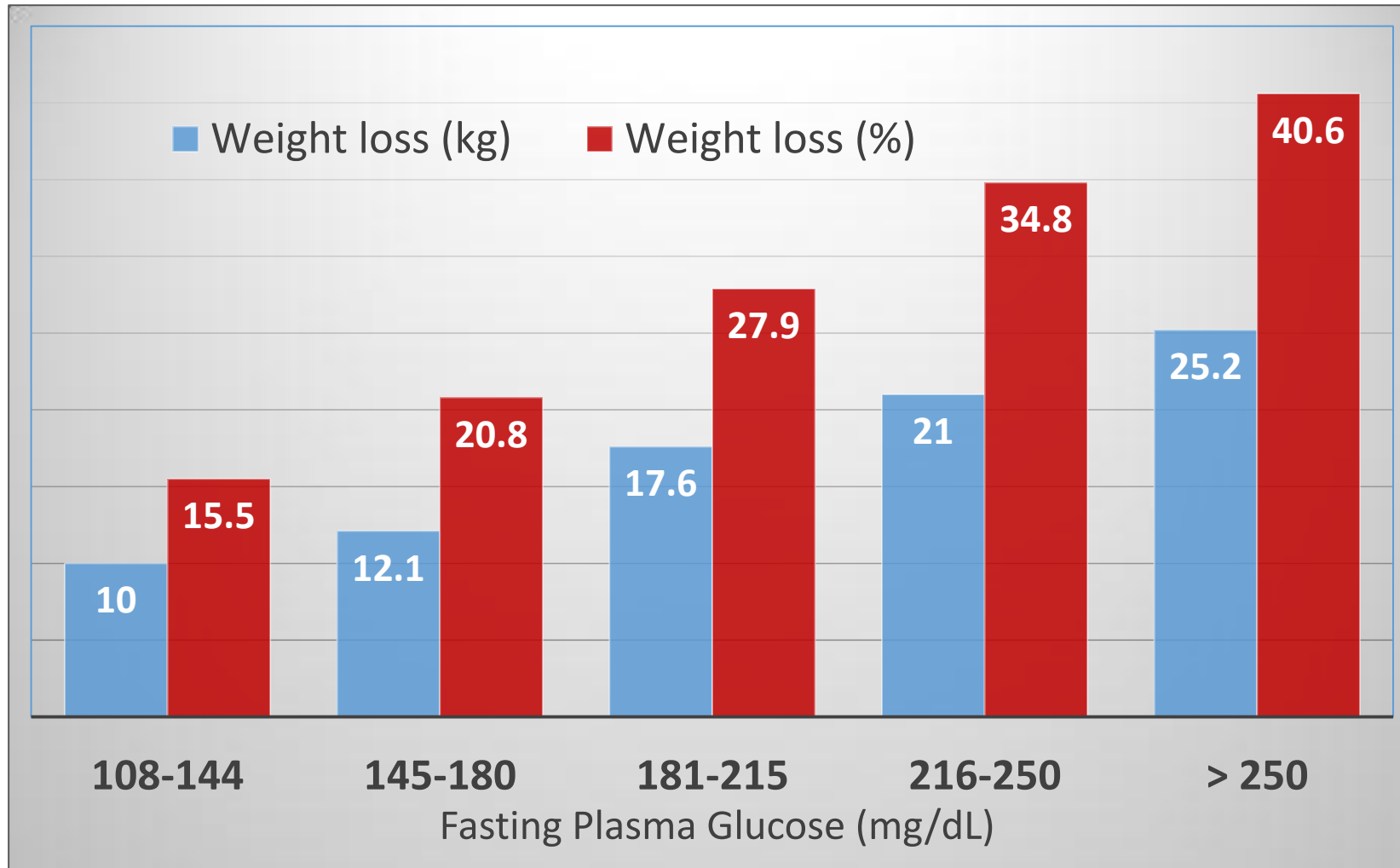
- Disease regression (A1C \leq 6.5% without medications) was uncommon, but once achieved, about 67% remained in remission for 4 years. Factors predicting success included baseline A1c $<$ 7.5% and diabetes duration $<$ 5 years¹
- Remission of OSA at 4 years was 5 times more common with intensive lifestyle intervention (20.7%) than diabetes support and education (3.6%)²
- Study stopped October 2012 due to failure to show CVD benefit (median follow-up 9.6 yrs)³

Weight Loss >5% Improves Comorbid Disease

- Improves glycemic control
- Increases life expectancy
- Lowers blood pressure
- Improves serum lipid profile
- May decrease cancer risk
- Improves lower back pain, reflux, lower extremity arthralgias, sleep apnea
- Can decrease drugs for obesity-related conditions



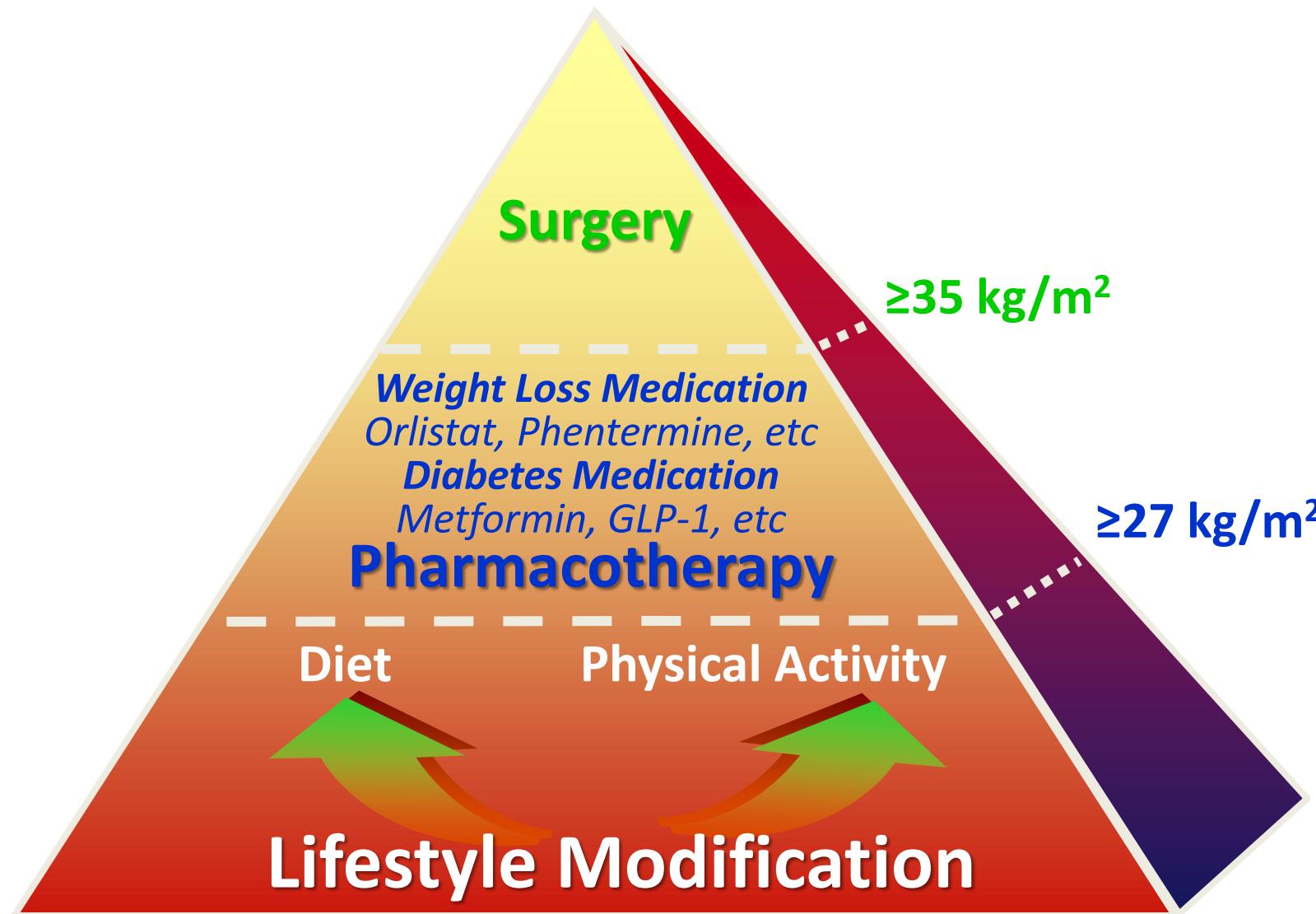
Weight Loss Required for Normoglycemia in Untreated Type 2 DM is Influenced by Initial FPG



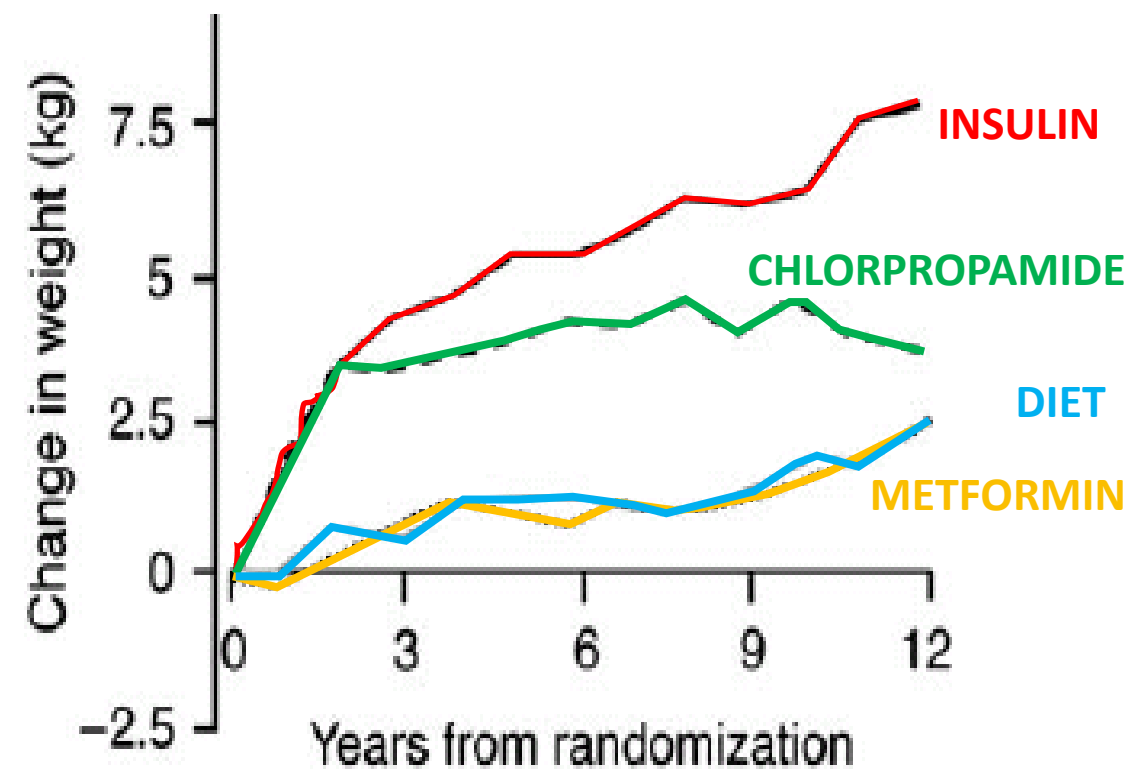
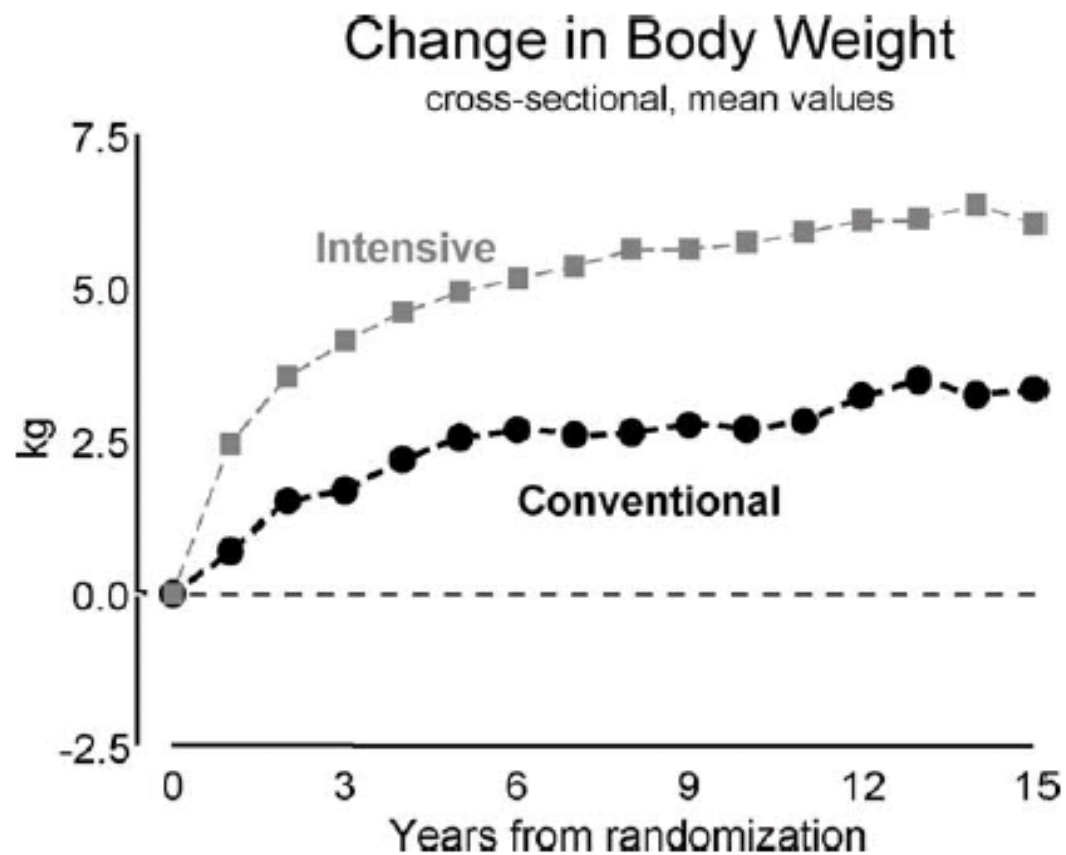
Treatment of Diabetes in the Obese Patient



Obesity-Focused Diabetes Management



UKPDS: Weight Gain with Intensive or Conventional T2DM Treatment is Greatest with Insulin Therapy



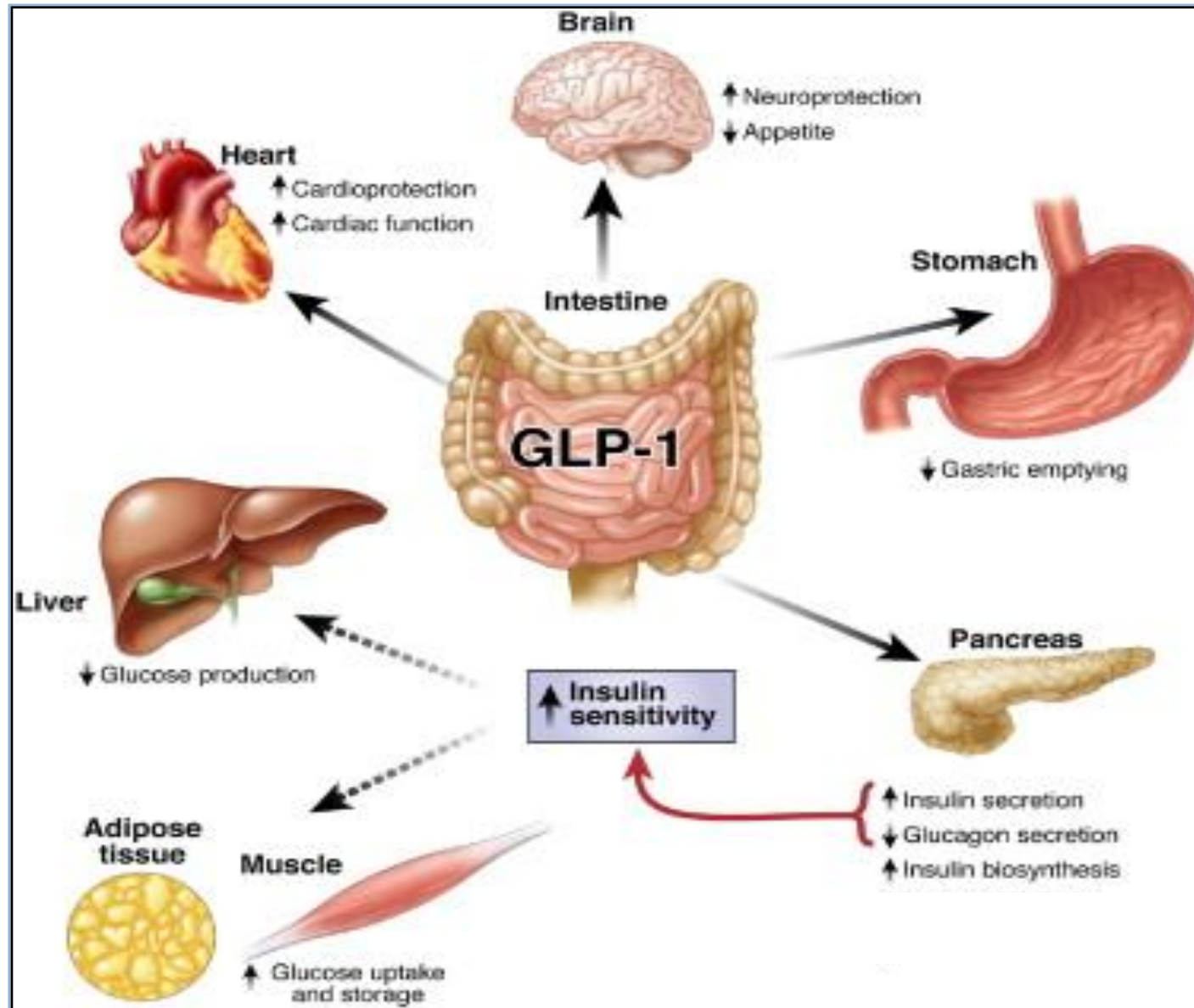
Approved Diabetes Medications

Class	Mechanism	Impact on FBG (mg/dL)	Impact on Hgb A1c	Impact on Weight (lbs)	Primary Side Effects
Amylin analog	Slows gastric emptying	-15 to 20	-0.4 to 0.6	-2.1 to 3.8	GI
α -glucosidase inhibitor	Delays glucose absorption in SI	-25 to 30	-0.5 to 0.8	+0.0 to 0.44	GI
DPP-4 inhibitor	↑ GLP-1	-17 to 20	-0.6 to 0.8	+0.0 to 0.8	GI, URI symptoms
GLP-1 agonist	↑ Insulin secretion, ↓ glucagon	-14 to 25	-0.5 to 1.0	-2.8 to 6.6	Nausea, GI
SGLT2 Inhibitor	↑ glucosuria	-24 to -39	-0.6 to 1.2	-6.1 to 8.3	UTI, yeast infections
Thiazolidinedione	+ insulin sensitivity	-60 to 80	-0.5 to 1.5	+9.2 to 10.6	Edema, wt gain
Meglitinide	↑ Insulin	-65 to 75	-0.5 to 2.0	+1.5 to 3.9	Hypoglycemia, wt gain
Sulfonylurea	↑ Insulin	-60 to 70	-0.8 to 2.0	+3.5 to 5.7	Hypoglycemia, wt gain
Biguanide (Metformin)	↓ hepatic glucose, + insulin sensitivity	-50 to 70	-1.0 to 2.0	-10.1 to +0.9	GI, lactic acidosis
Insulin	Replacement	>50	>2.0	+8.8 to 11.0	Hypoglycemia

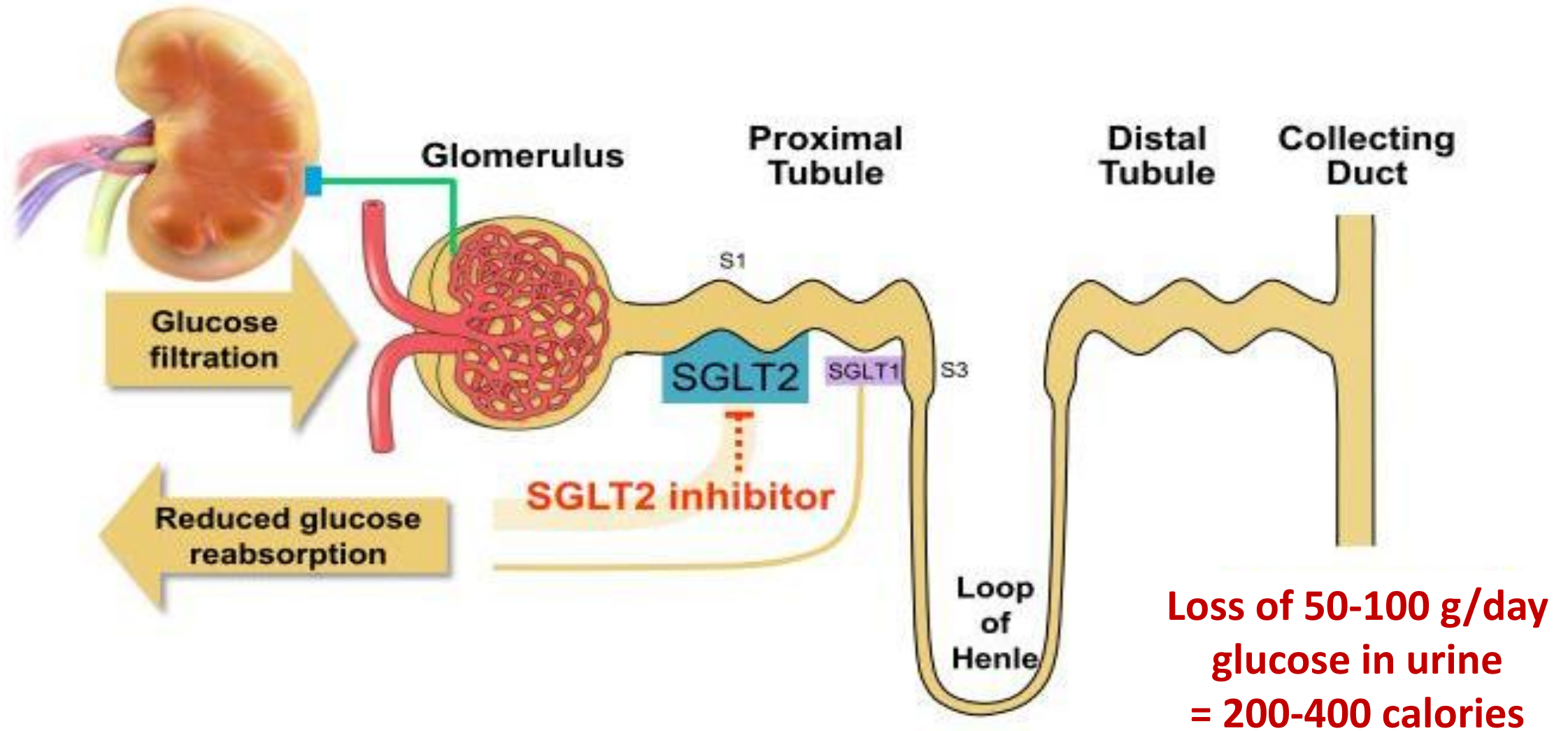
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Amylin analog	Slows gastric emptying	-15 to 20	-0.4 to 0.6	-2.1 to 3.8 ↓
α-glucosidase inhibitor	Delays glucose absorption in SI	-25 to 30	-0.5 to 0.8	+0.0 to 0.44 ↔
DPP-4 inhibitor	↑ GLP-1	-17 to 20	-0.6 to 0.8	+0.0 to 0.8 ↔
GLP-1 agonist	↑ Insulin secretion, ↓ glucagon	-14 to 25	-0.5 to 1.0	-2.8 to 6.6 ↓
SGLT2 Inhibitor	↑ glucosuria	-24 to -39	-0.6 to 1.2	-6.1 to 8.3 ↓
Thiazolidinedione	+ insulin sensitivity	-60 to 80	-0.5 to 1.5	+9.2 to 10.6 ↑
Meglitinide	↑ Insulin	-65 to 75	-0.5 to 2.0	+1.5 to 3.9 ↑
Sulfonylurea	↑ Insulin	-60 to 70	-0.8 to 2.0	+3.5 to 5.7 ↑
Biguanide (Metformin)	↓ hepatic glucose, + insulin sensitivity	-50 to 70	-1.0 to 2.0	-10.1 to +0.9 ↓
Insulin	Replacement	>50	>2.0	+8.8 to 11.0 ↑

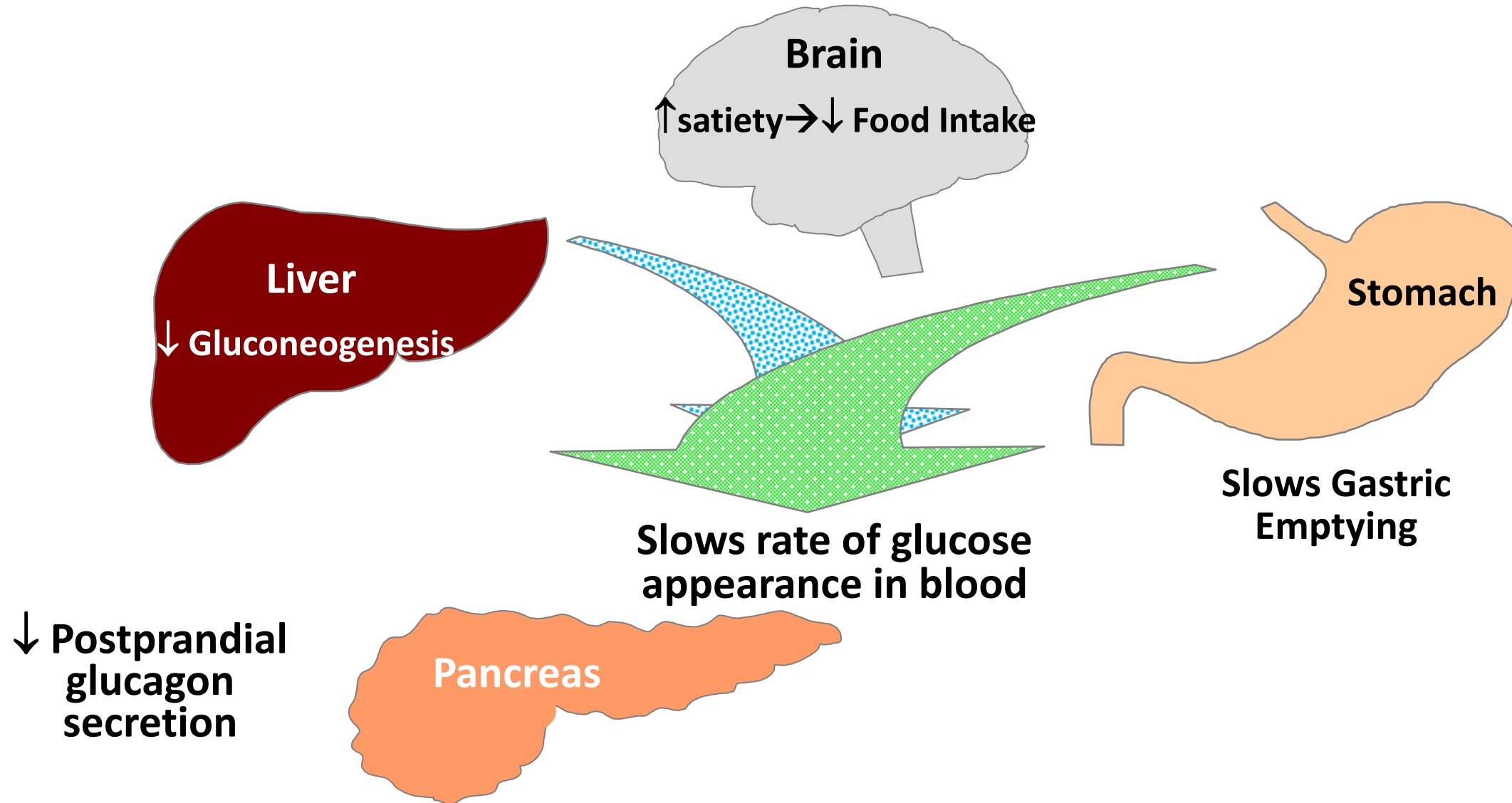
Physiologic Effects of GLP1



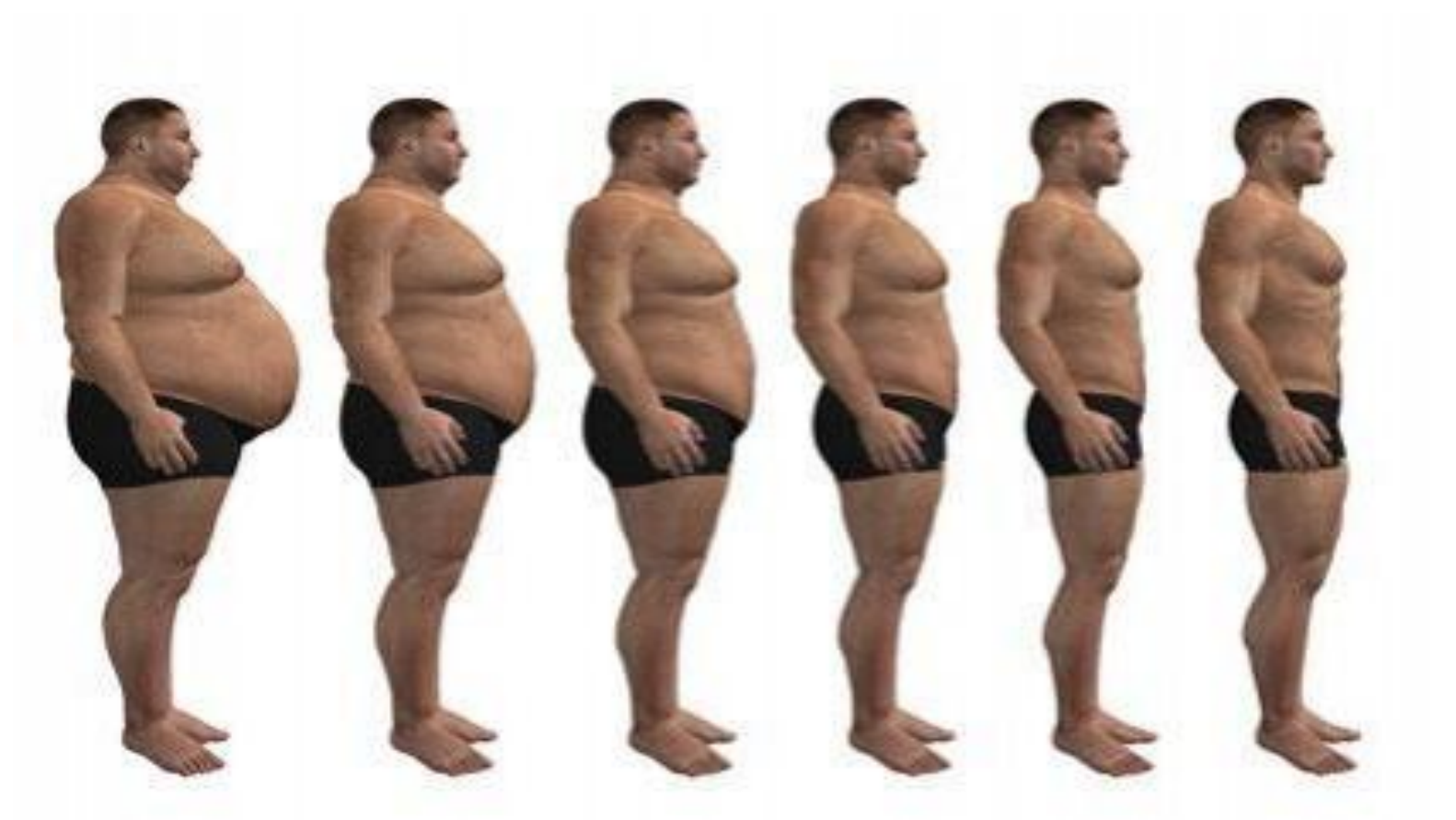
SGLT2 Inhibitors



AMYLIN : MECHANISM OF ACTION



Weight Loss Medication



Weight Loss Drugs Approved for Long Term Use

Drug	Net loss (kg)	Mechanism	Side Effects	Contraindications
Orlistat	3	Pancreatic lipase inhibitor	Gas, diarrhea, leakage of oily stool, rare liver damage	Chronic malabsorption, cholestasis
Lorcaserin (Belviq)	4.8	Serotonin-2C receptor agonist	Headache, dizziness, fatigue, nausea, dry mouth, constipation, rare serotonin syndrome	Use of other serotonergic agents or antidopaminergic agents
Topiramate/ phentermine (Qsymia)	12.2	Antiseizure/ Noradrenergic sympathomimetic	Headache, paraesthesia, ↑HR, ↑BP, dizziness, URI sx, insomnia, constipation, dry mouth	CVD, poorly controlled HTN, hyperthyroidism, glaucoma, MAOI use within 14 days

Weight Loss Drugs Approved for Short Term Use

Noradrenergic Sympathomimetic

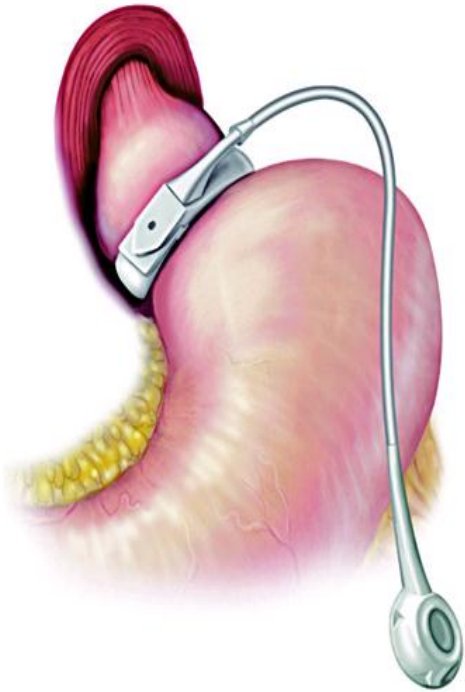
Drug	Side Effects	Contraindicated
Phentermine Diethylpropion Benzphetamine Phendimetrazine	↑HR, ↑BP, insomnia, dry mouth, constipation, nervousness. Abuse potential due to amphetamine-like effects	CVD, poorly controlled hypertension, pulmonary hypertension, hyperthyroidism, glaucoma, MAO inhibitor-therapy, agitated states, or history of addiction or drug abuse

Consider Obesity Pharmacotherapy

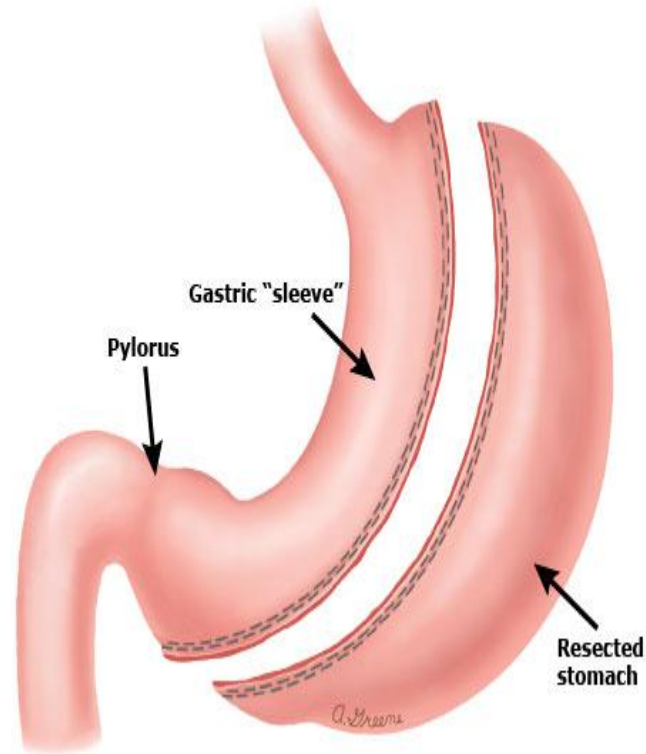
- Does patient with diabetes have a BMI ≥ 27 kg/m²?
- Are there any contraindications?
- Will medication enhance the likelihood of success?
- Consider adding in place of “traditional” diabetes medication
- Improves attrition and adherence rates



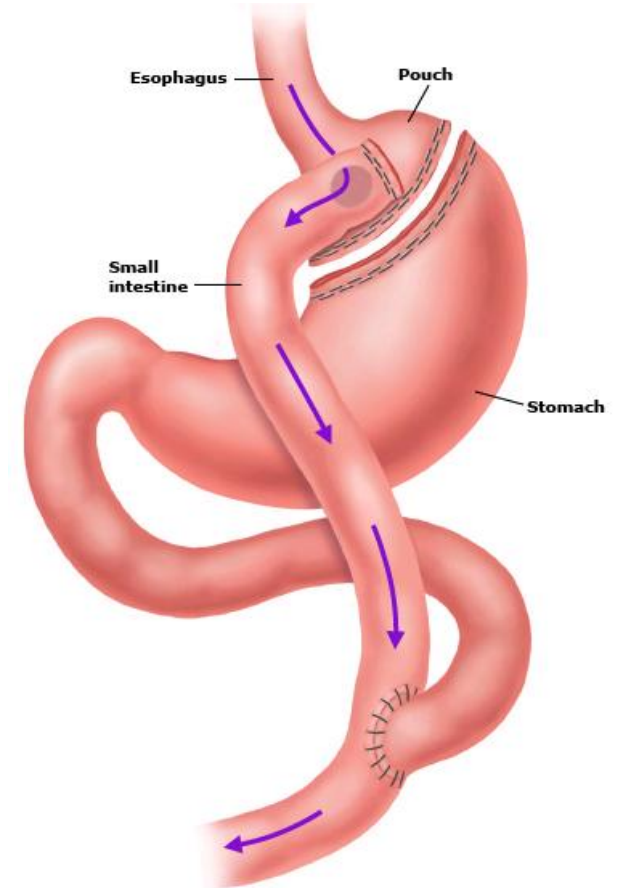
Bariatric Surgical Procedures



Adjustable gastric band

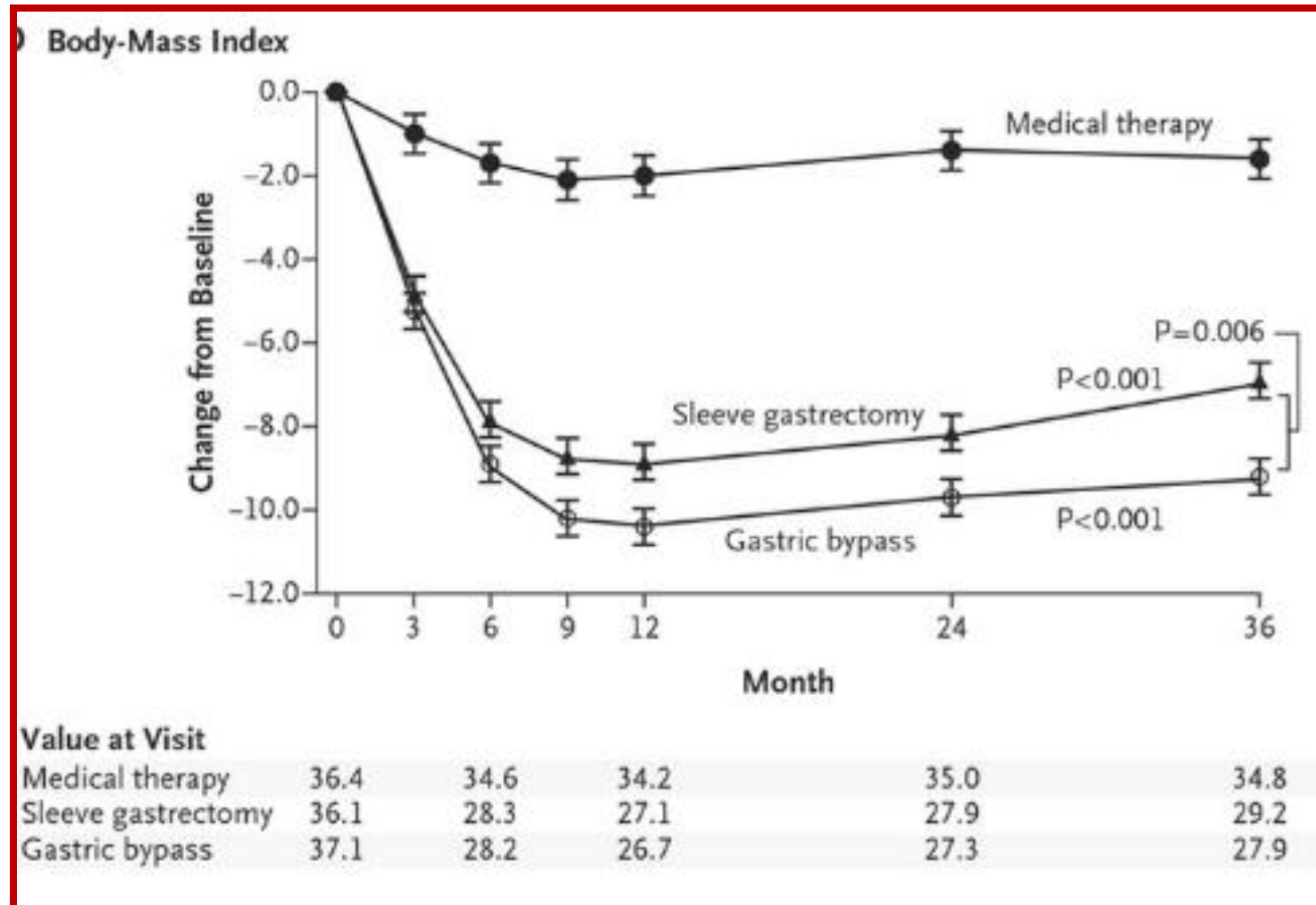


Sleeve gastrectomy

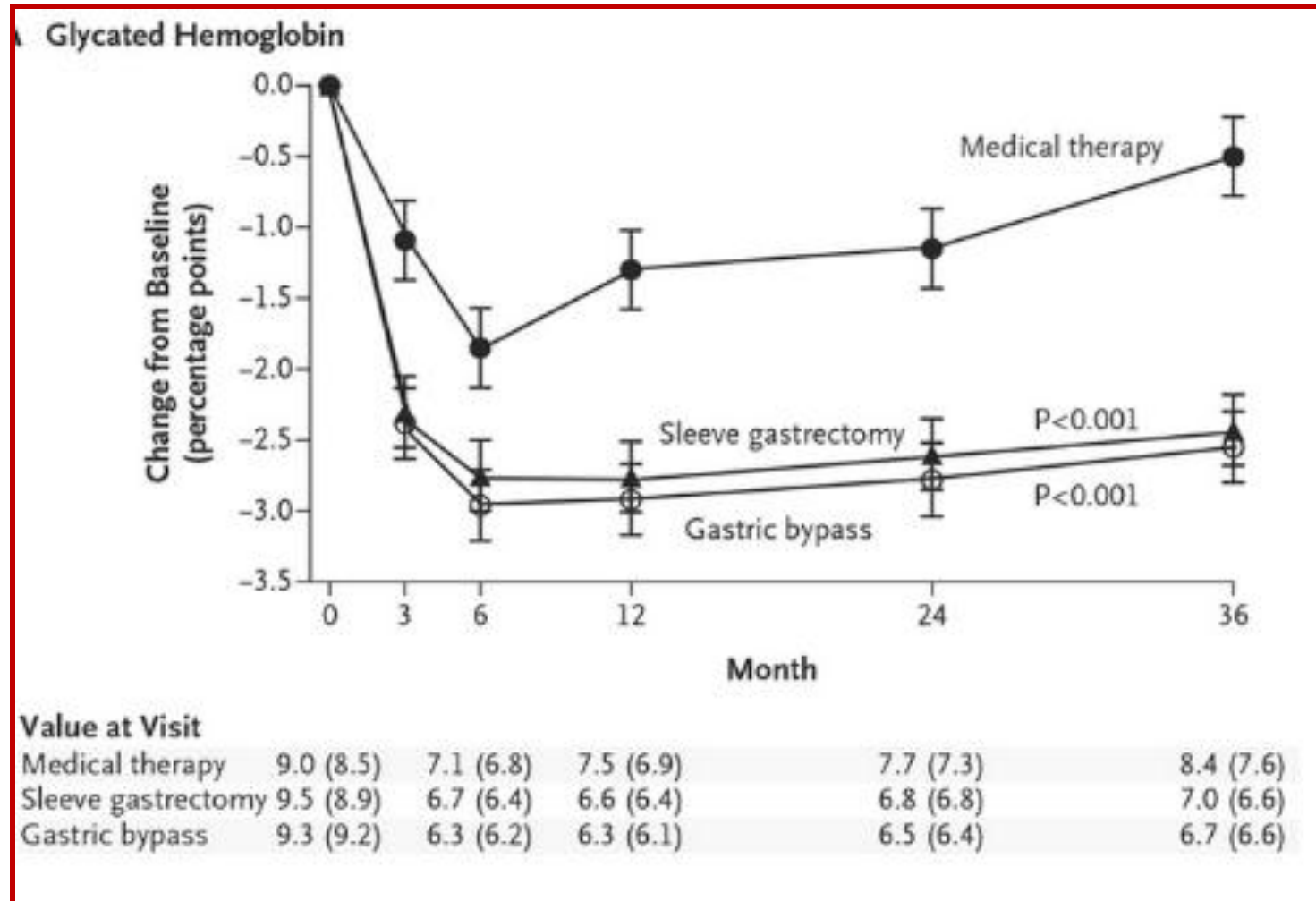


Roux-en-Y gastric bypass

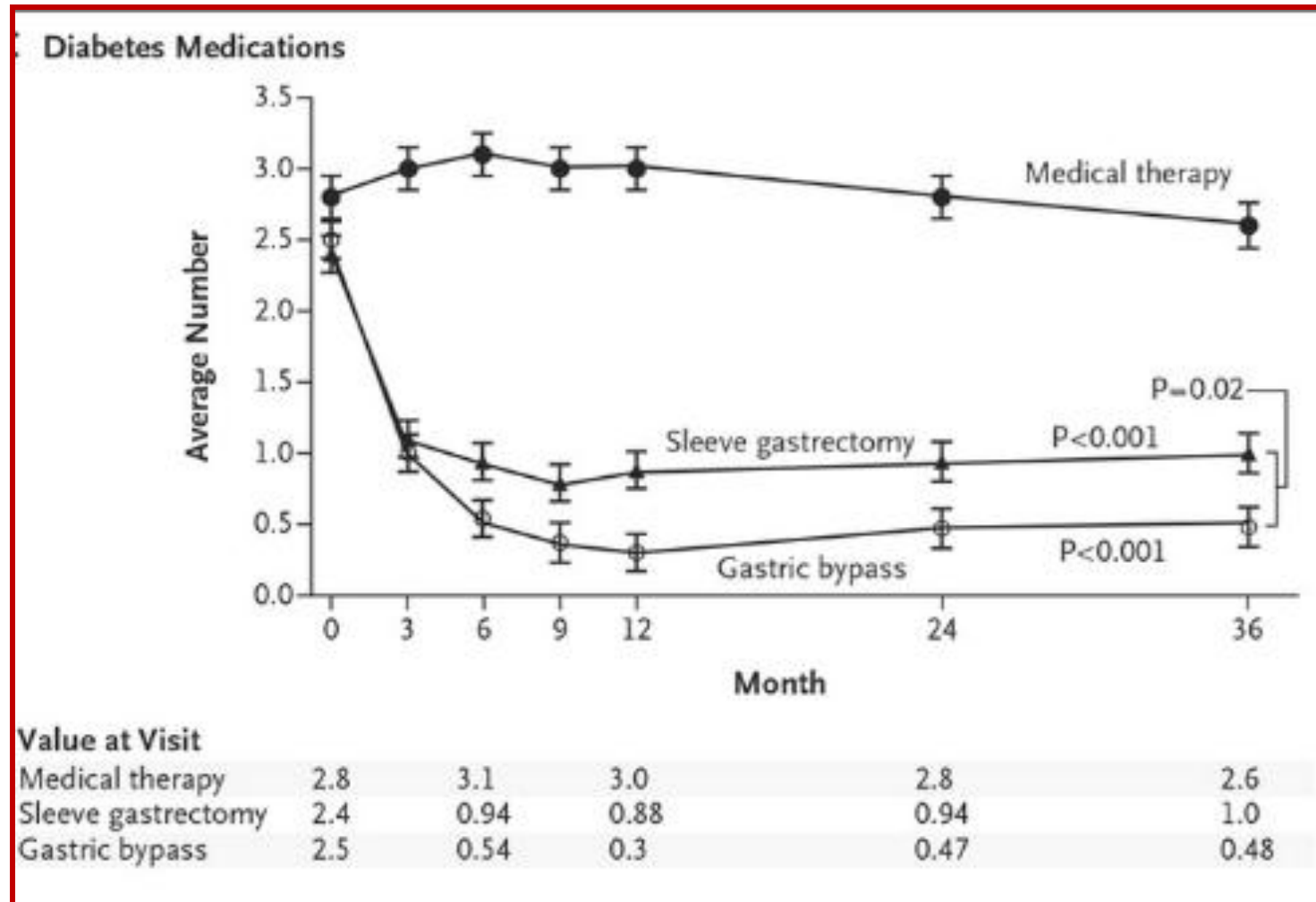
Bariatric Surgery vs. Medical Therapy for T2DM: BMI



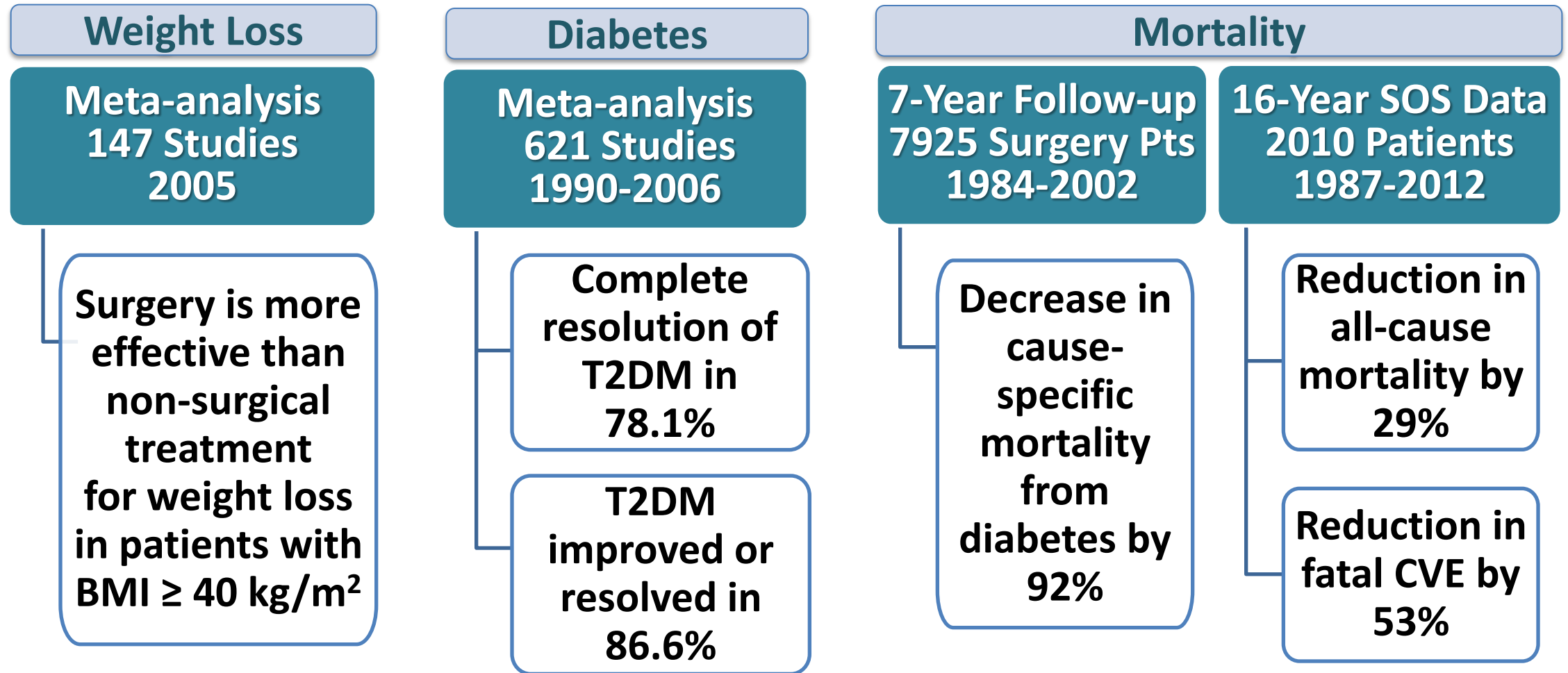
Bariatric Surgery vs. Medical Therapy for T2DM: HbA1c



Bariatric Surgery vs. Medical Therapy for T2DM: Diabetes Medications



Outcomes: Bariatric Surgery



NIH Guidelines for Obesity Surgery

- Weight loss surgery is an option in carefully selected patients with clinically severe obesity (BMI ≥ 40 or BMI ≥ 35 with comorbidity) when less invasive methods of weight loss have failed and the patient is at high risk for obesity-associated morbidity and mortality.
- “Failure” is ≥ 2 -5 years of medical therapy



QUESTIONS



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